Ultrashort Echo Time (UTE) Imaging of Myelin: T2* Analysis

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Target Audience: Neuroradiologists, Neurologists, White Matter Investigators

Introduction: Multiple sclerosis (MS) damages myelin of the central nervous system; this tissue has an extremely short T_2* and is not detected with conventional clinical MR sequences. Recent studies on high performance NMR spectrometers indicate that myelin has a T_2* of around fifty to few hundred microseconds[1-3]. We have developed adiabatic inversion recovery prepared ultrashort echo time (IR-UTE) sequences with a nominal TE of 8 µs, which can potentially detect signal from myelin using clinical MR scanners[4-6]. In this study we first evaluated UTE sequences for direct imaging and quantitative T_2* characterization of purified bovine myelin extract using a whole-body clinical 3T MR scanner. We further investigated IR-UTE imaging of myelin in the white matter of the brain of cadaveric specimens with histopathologically confirmed MS, healthy volunteers, and patients with MS.

Material & Methods: Figure 1 shows the IR-UTE sequence and contrast mechanism. An adiabatic inversion pulse (duration = 8.64 ms) was used to invert and null the long T2 components in white matter using an appropriate combination of TR and TI. Subsequent UTE acquisition detects myelin, which was not inverted because of its extremely short T2*. The UTE and IR-UTE pulse sequences were first applied to 90% purified lyophilized bovine myelin extract powder (Sigma-Aldrich), then to cadaveric human brains with confirmed MS (n=5), and finally to healthy volunteers (n=5) and MS patients (n=5). Typical imaging parameters in cadaver and live subjects were: FOV = 24 cm, slice thickness = 5 mm, bandwidth = 250 kHz, flip angle = 70°, TR = 1500 ms, TI ~ 420 ms (depending on T1 of long T2 white matter, which is measured with a 2D IR-FSE sequence), TE = 8 µs and 2.2 ms, 192 sampling points, 131 projections, recon matrix = 256×256, scan time = 6.5 min. Two to four sets of multi-echo IR-UTE acquisitions (e.g., TE = 0.008/2.2 ms; 0.2/2.2 ms; 0.6/2.2 ms; 1.5/4.4 ms) were acquired to quantify T2* with a total scan time of 26 min (specimens and volunteers) or 13 min (MS patients).

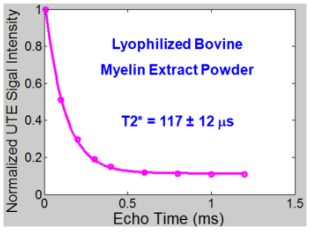

Fig 2 Signal versus TE of bovine myelin extract shows a T2* of 117 ± 12 µs at 3T.

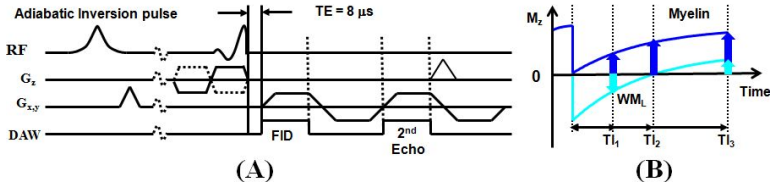

Fig 1 IR-UTE sequence. This employs half pulse excitation and dual echo radial ramp sampling preceded by an adiabatic IR pulse to invert and null the long T_2 white matter (WM_L), and saturate myelin. The myelin signal recovers during TI and is subsequently detected by UTE sampling. Contrast highly depends on TI (B). Too short a value of TI leads to myelin signal cancellation, while too long a TI leads to myelin signal overestimation. Optimal TI is related to the T1 of WM_L and TR.

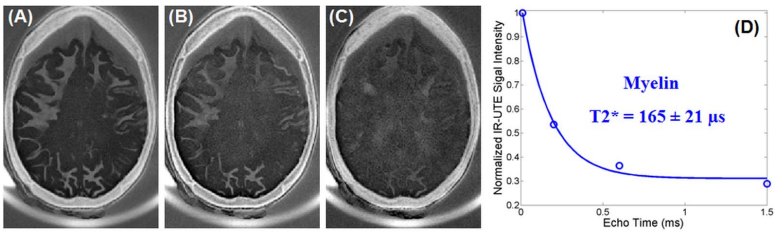

Fig 3 IR-UTE imaging of a MS brain with a TE of 8 µs (A), 0.2 ms (B), 0.6 ms (C). Exponential fitting shows a short T2* of 165 ± 21 µs (D), which is close to that of purified bovine myelin extract, suggesting that myelin can be imaged in vitro.

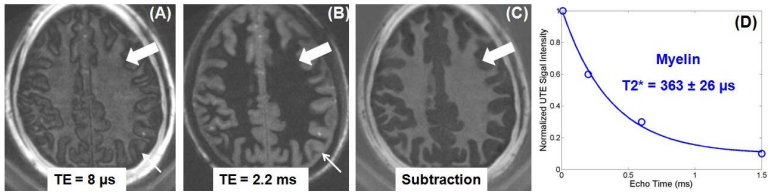

Fig 4 IR-UTE imaging of a healthy volunteer with TE's of 8 µs (A) and 2.2 ms (B). Subtraction of the second echo from the first suppresses residual signal from GM (thin arrow) and highlights myelin (thick arrow) (C). Exponential curve fitting shows a short T_2* of 363 ± 26 µs (D).

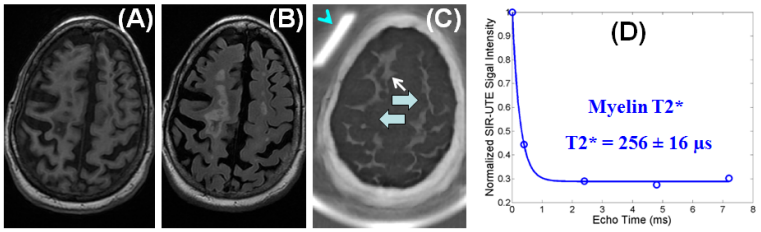

Fig 5 Clinical T2-FLAIR (A), MP-RAGE (B) and IR-UTE (C) imaging of a 69 year old female patient. The rubber phantom (arrow head) is only visible with UTE (C), and appears as very high signal. IR-UTE shows obvious myelin signal loss (thick arrows). The remaining myelin (e.g., thin arrow) has a short T2* of 256 ± 16 µs (D).

Results: Figure 2 shows UTE imaging of 90% purified lyophilized bovine myelin extract powder (Sigma-Aldrich). A short T_2* of 117 ± 12 µs is demonstrated with UTE and 115 ± 10 µs with IR-UTE imaging. **Figure 3** shows images of a MS brain from a 28y female cadaveric donor. Myelin shows a short T_2* of 165 ± 21 µs, which is comparable to that of purified bovine myelin extract, suggesting myelin can be directly imaged and quantified in vitro using clinical MR scanners. **Figure 4** shows IR-UTE imaging of a 60y old normal volunteer. Exponential signal decay fitting showed a T_2* of 363 ± 26 µs for myelin, which is more than twice the T_2* of myelin in the MS brain specimens. On average myelin in healthy volunteers have a short T_2* of 332 ± 34 µs. **Figure 5** shows representative T_2* measurement of a 69y old patient in a total scan time of 13 minutes. Again there is a fast signal decay for myelin in this patient, with a short T_2* of 256 ± 16 µs. This is consistent with values derived from cadaveric human brain donor specimens with confirmed MS.

Discussion: A trend of reduced T_2* was observed for myelin in MS specimens (mean T2* ~ 176 µs) and patients with MS (mean T2* ~ 241 µs) when compared with that in healthy volunteers (mean T2* ~332 µs), suggesting that T_2* is a potential biomarker for myelin status. Sites of MS lesions show reduced myelin signal.

Conclusions: Our study suggests that myelin is detectable with IR-UTE sequences on clinical scanners. Preliminary results show obvious myelin loss in brains of cadaveric MS specimens and patients, as well as a trend of reduction in T_2* values. IR-UTE sequences open the possibility of directly visualizing damage to myelin.

References

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